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10/573,093	03/23/2006	Nicholas Peter Franks	YOUZ 2 00116	8953

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EXAMINER	
ARNOLD, ERNST V	

ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/573,093	FRANKS ET AL.	
	Examiner	Art Unit	
	Ernst V. Arnold	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 9/19/07.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 20-41,44 and 46-49 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 20-41,44 and 46-49 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 9/19/07.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-19, 42-43 and 45 have been cancelled. Claims 46-49 are new. Claims 20-41, 44 and 46-49 are under examination.

Applicant's amendment has necessitated a new ground of rejection. Accordingly, this action is FINAL.

Comment: In claims 33 and 34, "hypoxic-ischemic (HI)" is recited. This is not literally recited in claim 20 but refers to the neonatal asphyxia. Support is given on page 1, line 6 of the specification which recites "Neonatal (or perinatal) asphyxia, also known as hypoxia-ischemia (HI)...". However, this language is awkward and the Examiner requests for clarity that the claim language be amended to reflect the synonymous meaning of the terms.

Withdrawn rejections:

Claim 38 was objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant has amended the claims and the objection is withdrawn.

Claims 1, 42 and 43 were rejected under 35 U.S.C. § 101 as being drawn to use claims, which are non-statutory process claims, as defined in 35 U.S.C. § 101. See, *Ex parte Dunki*, 153 USPQ 678 (Bd. App. 1967). In addition, claims 1, 42 and 43 were also rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicant has cancelled these claims rendering the rejections moot.

Claim 39 was rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. Claim 39 recites the limitation "sub-therapeutically effective amount" in line 2. There is insufficient antecedent basis for this limitation in the claim. Applicant has amended the claims and the Examiner withdraws the rejections.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 39 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 39 and 49 recite "sub-therapeutically effective amount". It is unclear to the Examiner what exactly is meant by this term because the xenon must be at some therapeutically effective amount in conjunction with the hypothermia in order for this invention to work. The rejection could be overcome by amending the independent claims to recite the exact amount of xenon used to obtain the synergistic results.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter

sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 20-41, 44 and 46-49 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over Fishman (US 5,099,834) in view of Georgieff (US 6,197,323) and Taylor et al. (Pediatric Research 2002, 51(1), 13-19) and Ohashi et al. Anesthesiology 2002, 96, A1291.

Applicant claims a method of treating neonatal asphyxia in a mammal in need thereof comprising administering a therapeutically effective amount of xenon to the mammal; and subjecting the mammal to hypothermia.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Fishman teaches administration of xenon gas mixtures, from 60 to 78.5 mole percent xenon, to women of childbearing age (Abstract and claims 1-14). Fishman teaches that nitrous oxide is toxic to a fetus (column 1, lines 49-60). Fishman teach a mixture consisting of from 60 to 78.5 mole percent stable xenon, from 19.5 to 38 mole percent oxygen and from 2.5 to 20.5

mole percent helium (Claim 1). Methods of making and methods of using the gas mixture are disclosed (Column 3, lines 14-42 and column 5, lines 8-36) and use of the gas mixture in combination with intravenously introduced methyl-atrophine bromide, thiopentone and fentanyl (Column 5, lines 10-13). It is the Examiner's position that any xenon administered to pregnant women would also be administered to the unborn child.

Georgieff teaches liquid anesthetic lipophilic gas preparations and methods of inducing analgesia comprising xenon and in a fatty emulsion (excipient/carrier) that can be administered intravenously or by inhalation (Abstract; column 9, lines 10-16; column 10, lines 22-65 and claims 16). Georgieff teach ointments and creams which can be applied to the damaged tissue thus reading on transdermal application (column 9, lines 40-54). Georgieff teaches that any known inhalation anesthetic, such as sevoflurane, desflurane and isoflurane, can be combined with the xenon fatty emulsion (Column 8, lines 9-16). Sub-anesthetic amounts are also contemplated by Georgieff (Column 7, lines 33-40).

Taylor et al. teach improved neuroprotection with hypothermia following cerebral hypoxia-ischemia in the rat (title). Taylor et al. teach cooling the rat to brain temperatures of 30 C or 33 C for up to 12 hours after hypoxia (Abstract). Cooling between 6 and 12 hours after hypoxia-ischemia is more effective in reducing cerebral injury than other cooling regimes (Abstract). Taylor et al. teach that the results have implications for application in birth asphyxia (Page 19, left column middle of page).

Ohashi et al. disclose treating newborn Fischer rats, to test the antinociceptive effect of xenon, with either air or xenon (± 75% v/v). Air is a diluent and carrier for the xenon.

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

1. Fishman does not expressly teach a method of treating neonatal asphyxia in a mammal in need thereof comprising administering a therapeutically effective amount of xenon to the mammal and subjecting the mammal to hypothermia; 20 to70 % v/v xenon/air mixture; administration of xenon in the form of a lipid emulsion or where xenon is administered by perfusion, intravenously, neuraxially or transdermally; simultaneously, sequentially or separately with hypothermia; where the temperature is maintained from about 33 to about 35 C; for a period of at least 6 hours after the hypoxic-ischemic insult; for a period form about 6 to about 24 hours after the insult; administration of xenon to the mother prior to labour, administration of xenon to the mother prior to, or during labour for up to 24 hours prior to birth in a therapeutic; and where the xenon is co-administered with an anesthetic selected from isoflurane, sevoflurane and desflurane.

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

1. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the methods of Fishman and Taylor et al. to arrive at a method of treating neonatal asphyxia in a mammal in need thereof comprising administering a therapeutically effective amount of xenon to the mammal and subjecting the mammal to hypothermia wherein there is a xenon gas mixture of 20 to 70% v/v xenon air, as suggested by Ohashi et al., or administer the xenon in the form of lipid emulsion intravenously, as suggested

by Georgieff, by perfusion, simultaneously, sequentially or separately with hypothermia; where the temperature is maintained from about 33 to about 35 C, as taught by Taylor et al., for a period of at least 6 hours after the hypoxic-ischemic insult; for a period form about 6 to about 24 hours after the insult, as taught by Taylor et al., administration of xenon to the mother prior to birth, administration of xenon to the mother prior to, or during labour for up to 24 hours prior to birth in a therapeutic or sub-therapeutic amount, as taught by Georgieff, and where the xenon is co-administered with an anesthetic selected from isoflurane, sevoflurane and desflurane, as taught by Georgieff, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because: 1) Fishman teach administration of xenon to women of child bearing age for protection of the unborn child and 2) Taylor et al. suggest hypothermic treatment in rescue therapies of birth asphyxia (page 19, middle of page). One of ordinary skill in the art would select and administer the xenon to the mother or the newborn mammal to avoid the risk of toxic nitrous oxide to the newborn mammal. It is merely a matter treatment choice by one of ordinary skill in the art to select when to administer the xenon, in which form, such as an emulsion, in combination with other medicaments and at what temperature and duration to maintain the hypothermia. Ohashi et al. suggest ±75% xenon/air mixture and it is merely routine optimization to arrive at the instantly claimed 70% xenon/air mixture. One of ordinary skill in the art would recognize other means of providing analgesia to a patient such as intravenous administration of xenon in a carrier as taught by Georgeiff. One of ordinary skill in the art would be motivated to use xenon, in such alternative forms in addition to inhalation, because nitrous oxide is taught by Fishman to be toxic to an unborn mammal. So, one of ordinary skill in the art would be motivated to administer a

therapeutically effective amount of xenon to women of childbearing age, and thus the unborn child as well as directly to the child once born. The route of administration and timing of administration is easily determined by one of ordinary skill in the art. The unborn mammal would intrinsically benefit from any properties of the gas.

Objective evidence of nonobviousness, if any, must be commensurate in scope with that of the claimed subject matter. In re Kulling, 14 USPQ2d 1056 (Fed. Cir. 1990); In re Lindner, 173 USPQ 356 (CCPA 1972).

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to arguments:

Applicants assert that the administration of xenon with hypothermia produces unexpected synergistic results. The Examiner appreciates the results obtained by Applicant. However, the claim language is not commensurate in scope with the unexpected results. This rejection is based on the well established proposition of patent law that no invention resides in combining old components/techniques of known properties where the results obtained thereby are no more than the additive effect of the ingredients. Applicants invention is predicated on an unexpected result, which involves synergism, an unpredictable phenomenon, highly dependent upon specific

proportions and/or amounts of particular ingredients. Any mixture of the components embraced by the claims, which does not exhibit an unexpected result (e.g., synergism) is therefore ipso facto unpatentable.

Further, with regards to the synergistic effects, it is noted that the features upon which applicant relies (i.e., a synergistic effect) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Accordingly, the instant claims, in the range of proportions where no unexpected results are observed would have been obvious to one of ordinary skill having the above cited references before him.

Objective evidence of nonobviousness, if any, must be commensurate in scope with that of the claimed subject matter. In re Kulling, 14 USPQ2d 1056 (Fed. Cir. 1990); In re Lindner, 173 USPQ 356 (CCPA 1972).

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ernst V. Arnold whose telephone number is 571-272-8509. The examiner can normally be reached on M-F (6:15 am-3:45 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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